



SEQUENCE LISTING

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<120> CRYSTAL STRUCTURE OF BACE AND USES
THEREOF

<130> 16163-015001

<140> US 09/955,737

<141> 2001-09-19

<150> US 60/234,576

<151> 2000-09-22

<160> 15

<170> FastSEQ for Windows Version 4.0

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<212> PRT

<213> Homo sapiens

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Gly	Leu	Gly	Gly	Ala	Pro	Leu	Gly	Leu	Arg	Leu	Pro	Arg	Glu	Thr	Asp
		35					40					45			
Glu	Glu	Pro	Glu	Glu	Pro	Gly	Arg	Arg	Gly	Ser	Phe	Val	Glu	Met	Val
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Asp	Asn	Leu	Arg	Gly	Lys	Ser	Gly	Gln	Gly	Tyr	Tyr	Val	Glu	Met	Thr
65					70					75				80	
Val	Gly	Ser	Pro	Pro	Gln	Thr	Leu	Asn	Ile	Leu	Val	Asp	Thr	Gly	Ser
			85						90					95	
Ser	Asn	Phe	Ala	Val	Gly	Ala	Ala	Pro	His	Pro	Phe	Leu	His	Arg	Tyr
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Tyr	Gln	Arg	Gln	Leu	Ser	Ser	Thr	Tyr	Arg	Asp	Leu	Arg	Lys	Gly	Val
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Tyr	Val	Pro	Tyr	Thr	Gln	Gly	Lys	Trp	Glu	Gly	Glu	Leu	Gly	Thr	Asp
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Leu	Val	Ser	Ile	Pro	His	Gly	Pro	Asn	Val	Thr	Val	Arg	Ala	Asn	Ile
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Ala	Ala	Ile	Thr	Glu	Ser	Asp	Lys	Phe	Phe	Ile	Asn	Gly	Ser	Asn	Trp
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Glu	Gly	Ile	Leu	Gly	Leu	Ala	Tyr	Ala	Glu	Ile	Ala	Arg	Pro	Asp	Asp
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Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro
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Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln
    210                215                220
Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile
    225                230                235                240
Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg
    245                250                255
Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln
    260                265                270
Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val
    275                280                285
Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala
    290                295                300
Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp
    305                310                315                320
Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr
    325                330                335
Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val
    340                345                350
Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg
    355                360                365
Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala
    370                375                380
Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu
    385                390                395                400
Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala
    405                410                415
Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu
    420                425                430
Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro
    435                440                445
Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala
    450                455                460
Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp
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Arg Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp
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Ile Ser Leu Leu Lys
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<212> PRT
<213> Homo sapiens

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Gln Ile Ala Met Phe Cys Gly Arg Leu Asn Met His Met Asn Val Gln
    35          40          45
Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp
    50          55          60
Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu
    65          70          75          80

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Gln	Ile	Thr	Asn	Val	Val	Glu	Ala	Asn	Gln	Pro	Val	Thr	Ile	Gln	Asn
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Ile	Pro	Tyr	Arg	Cys	Leu	Val	Gly	Glu	Phe	Val	Ser	Asp	Ala	Leu	Leu
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Val	Pro	Asp	Lys	Cys	Lys	Phe	Leu	His	Gln	Glu	Arg	Met	Asp	Val	Cys
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Glu	Thr	His	Leu	His	Trp	His	Thr	Val	Ala	Lys	Glu	Thr	Cys	Ser	Glu
145					150					155					160
Lys	Ser	Thr	Asn	Leu	His	Asp	Tyr	Gly	Met	Leu	Leu	Pro	Cys	Gly	Ile
			165					170						175	
Asp	Lys	Phe	Arg	Gly	Val	Glu	Phe	Val	Cys	Cys	Pro	Leu	Ala	Glu	Glu
			180					185					190		
Ser	Asp	Asn	Val	Asp	Ser	Ala	Asp	Ala	Glu	Glu	Asp	Asp	Ser	Asp	Val
		195					200					205			
Trp	Trp	Gly	Gly	Ala	Asp	Thr	Asp	Tyr	Ala	Asp	Gly	Ser	Glu	Asp	Lys
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Val	Val	Glu	Val	Ala	Glu	Glu	Glu	Glu	Val	Ala	Glu	Val	Glu	Glu	Glu
225					230					235					240
Glu	Ala	Asp	Asp	Asp	Glu	Asp	Asp	Glu	Asp	Gly	Asp	Glu	Val	Glu	Glu
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Glu	Ala	Glu	Glu	Pro	Tyr	Glu	Glu	Ala	Thr	Glu	Arg	Thr	Thr	Ser	Ile
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Ala	Thr	Thr	Thr	Thr	Thr	Thr	Thr	Glu	Ser	Val	Glu	Glu	Val	Val	Arg
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Val	Pro	Thr	Thr	Ala	Ala	Ser	Thr	Pro	Asp	Ala	Val	Asp	Lys	Tyr	Leu
		290				295					300				
Glu	Thr	Pro	Gly	Asp	Glu	Asn	Glu	His	Ala	His	Phe	Gln	Lys	Ala	Lys
305					310					315					320
Glu	Arg	Leu	Glu	Ala	Lys	His	Arg	Glu	Arg	Met	Ser	Gln	Val	Met	Arg
			325					330						335	
Glu	Trp	Glu	Glu	Ala	Glu	Arg	Gln	Ala	Lys	Asn	Leu	Pro	Lys	Ala	Asp
			340					345					350		
Lys	Lys	Ala	Val	Ile	Gln	His	Phe	Gln	Glu	Lys	Val	Glu	Ser	Leu	Glu
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Gln	Glu	Ala	Ala	Asn	Glu	Arg	Gln	Gln	Leu	Val	Glu	Thr	His	Met	Ala
		370				375					380				
Arg	Val	Glu	Ala	Met	Leu	Asn	Asp	Arg	Arg	Arg	Leu	Ala	Leu	Glu	Asn
385					390					395					400
Tyr	Ile	Thr	Ala	Leu	Gln	Ala	Val	Pro	Pro	Arg	Pro	Arg	His	Val	Phe
			405					410						415	
Asn	Met	Leu	Lys	Lys	Tyr	Val	Arg	Ala	Glu	Gln	Lys	Asp	Arg	Gln	His
			420					425					430		
Thr	Leu	Lys	His	Phe	Glu	His	Val	Arg	Met	Val	Asp	Pro	Lys	Lys	Ala
		435					440					445			
Ala	Gln	Ile	Arg	Ser	Gln	Val	Met	Thr	His	Leu	Arg	Val	Ile	Tyr	Glu
		450				455					460				
Arg	Met	Asn	Gln	Ser	Leu	Ser	Leu	Leu	Tyr	Asn	Val	Pro	Ala	Val	Ala
465					470					475					480
Glu	Glu	Ile	Gln	Asp	Glu	Val	Asp	Glu	Leu	Leu	Gln	Lys	Glu	Gln	Asn
			485					490						495	
Tyr	Ser	Asp	Asp	Val	Leu	Ala	Asn	Met	Ile	Ser	Glu	Pro	Arg	Ile	Ser
			500					505					510		
Tyr	Gly	Asn	Asp	Ala	Leu	Met	Pro	Ser	Leu	Thr	Glu	Thr	Lys	Thr	Thr
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Val	Glu	Leu	Leu	Pro	Val	Asn	Gly	Glu	Phe	Ser	Leu	Asp	Asp	Leu	Gln

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545	550	555
Glu Val Glu Pro Val Asp Ala Arg Pro Ala	Ala Asp Arg Gly Leu Thr	560
	565	570
Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile	Lys Thr Glu Glu Ile Ser	575
	580	585
Glu Val Lys Met Asp Ala Glu Phe Arg His	Asp Ser Gly Tyr Glu Val	590
	595	600
His His Gln Lys Leu Val Phe Phe Ala Glu	Asp Val Gly Ser Asn Lys	605
	610	615
Gly Ala Ile Ile Gly Leu Met Val Gly Gly	Val Val Ile Ala Thr Val	620
625	630	635
Ile Val Ile Thr Leu Val Met Leu Lys Lys	Lys Gln Tyr Thr Ser Ile	640
	645	650
His His Gly Val Val Glu Val Asp Ala Ala	Val Thr Pro Glu Glu Arg	655
	660	665
His Leu Ser Lys Met Gln Gln Asn Gly Tyr	Glu Asn Pro Thr Tyr Lys	670
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Phe Phe Glu Gln Met Gln Asn		685
690	695	

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<221> VARIANT

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<223> Xaa = Sta = Statine

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5

<210> 4

<211> 29

<212> DNA

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<223> Primer

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29

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<212> DNA

<213> Artificial Sequence

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<223> Primer

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<210> 7
<211> 390
<212> PRT
<213> Homo sapiens

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Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn
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Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro
35 40 45
His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr
50 55 60
Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp
65 70 75 80
Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn
85 90 95
Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe
100 105 110
Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala
115 120 125
Glu Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu
130 135 140
Val Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly
145 150 155 160
Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly
165 170 175
Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu
180 185 190
Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val
195 200 205
Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr
210 215 220
Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu
225 230 235 240
Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser
245 250 255
Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val
260 265 270
Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser

275					280					285					
Leu	Tyr	Leu	Met	Gly	Glu	Val	Thr	Asn	Gln	Ser	Phe	Arg	Ile	Thr	Ile
290					295					300					
Leu	Pro	Gln	Gln	Tyr	Leu	Arg	Pro	Val	Glu	Asp	Val	Ala	Thr	Ser	Gln
305					310					315					
Asp	Asp	Cys	Tyr	Lys	Phe	Ala	Ile	Ser	Gln	Ser	Ser	Thr	Gly	Thr	Val
325					330					335					
Met	Gly	Ala	Val	Ile	Met	Glu	Gly	Phe	Tyr	Val	Val	Phe	Asp	Arg	Ala
340					345					350					
Arg	Lys	Arg	Ile	Gly	Phe	Ala	Val	Ser	Ala	Cys	His	Val	His	Asp	Glu
355					360					365					
Phe	Arg	Thr	Ala	Ala	Val	Glu	Gly	Pro	Phe	Val	Thr	Leu	Asp	Met	Glu
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Asp	Cys	Gly	Tyr	Asn	Ile										
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<213> Homo sapiens
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Leu	Val	Asp 35	Thr	Gly	Ser	Ser	Asn 40	Phe	Ala	Val	Gly	Ala 45	Ala	Pro	His
Pro	Phe 50	Leu	His	Arg	Tyr	Tyr 55	Gln	Arg	Gln	Leu	Ser 60	Ser	Thr	Tyr	Arg
Asp 65	Leu	Arg	Lys	Gly	Val 70	Tyr	Val	Pro	Tyr	Thr 75	Gln	Gly	Lys	Trp	Glu 80
Gly	Glu	Leu	Gly	Thr 85	Asp	Leu	Val	Ser	Ile 90	Pro	His	Gly	Pro	Asn 95	Val
Thr	Val	Arg	Ala 100	Asn	Ile	Ala	Ala 105	Ile	Thr	Glu	Ser	Asp 110	Lys	Phe	Phe
Ile	Asn	Gly 115	Ser	Asn	Trp	Glu	Gly 120	Ile	Leu	Gly	Leu	Ala 125	Tyr	Ala	Glu
Ile	Ala 130	Arg	Pro	Asp	Asp	Ser	Leu 135	Glu	Pro	Phe	Phe 140	Asp	Ser	Leu	Val
Lys 145	Gln	Thr	His	Val	Pro	Asn 150	Leu	Phe	Ser	Leu 155	Gln	Leu	Cys	Gly	Ala 160
Gly	Phe	Pro	Leu	Asn 165	Gln	Ser	Glu	Val	Leu 170	Ala	Ser	Val	Gly	Gly 175	Ser
Met	Ile	Ile	Gly 180	Gly	Ile	Asp	His	Ser 185	Leu	Tyr	Thr	Gly	Ser 190	Leu	Trp
Tyr	Thr	Pro 195	Ile	Arg	Arg	Glu	Trp 200	Tyr	Tyr	Glu	Val	Ile 205	Ile	Val	Arg
Val	Glu 210	Ile	Asn	Gly	Gln	Asp 215	Leu	Lys	Met	Asp	Cys 220	Lys	Glu	Tyr	Asn
Tyr 225	Asp	Lys	Ser	Ile	Val 230	Asp	Ser	Gly	Thr	Thr 235	Asn	Leu	Arg	Leu	Pro 240
Lys	Lys	Val	Phe 245	Glu	Ala	Ala	Val	Lys	Ser 250	Ile	Lys	Ala	Ala 255	Ser	Ser
Thr	Glu	Lys	Phe 260	Pro	Asp	Gly	Phe	Trp 265	Leu	Gly	Glu	Gln	Leu 270	Val	Cys
Trp	Gln	Ala	Gly	Thr	Thr	Pro	Trp	Asn	Ile	Phe	Pro	Val	Ile	Ser	Leu

	275					280						285							
Tyr	Leu	Met	Gly	Glu	Val	Thr	Asn	Gln	Ser	Phe	Arg	Ile	Thr	Ile	Leu				
	290						295					300							
Pro	Gln	Gln	Tyr	Leu	Arg	Pro	Val	Glu	Asp	Val	Ala	Thr	Ser	Gln	Asp				
305					310					315					320				
Asp	Cys	Tyr	Lys	Phe	Ala	Ile	Ser	Gln	Ser	Ser	Thr	Gly	Thr	Val	Met				
				325					330					335					
Gly	Ala	Val	Ile	Met	Glu	Gly	Phe	Tyr	Val	Val	Phe	Asp	Arg	Ala	Arg				
			340					345					350						
Lys	Arg	Ile	Gly	Phe	Ala	Val	Ser	Ala	Cys	His	Val	His	Asp	Glu	Phe				
		355					360					365							
Arg	Thr	Ala	Ala	Val	Glu	Gly	Pro	Phe	Val	Thr	Leu	Asp	Met	Glu	Asp				
	370					375					380								
Cys	Gly	Tyr	Asn	Ile	Pro														
385					390														

<210> 9
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 <212> PRT
 <213> Homo sapiens

Gly	Ser	Phe	Val	Glu	Met	Val	Asp	Asn	Leu	Arg	Gly	Lys	Ser	Gly	Gln				
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Gly	Tyr	Tyr	Val	Glu	Met	Thr	Val	Gly	Ser	Pro	Pro	Gln	Thr	Leu	Asn				
			20					25				30							
Ile	Leu	Val	Asp	Thr	Gly	Ser	Ser	Asn	Phe	Ala	Val	Gly	Ala	Ala	Pro				
		35				40					45								
His	Pro	Phe	Leu	His	Arg	Tyr	Tyr	Gln	Arg	Gln	Leu	Ser	Ser	Thr	Tyr				
	50				55					60									
Arg	Asp	Leu	Arg	Lys	Gly	Val	Tyr	Val	Pro	Tyr	Thr	Gln	Gly	Lys	Trp				
65				70				75						80					
Glu	Gly	Glu	Leu	Gly	Thr	Asp	Leu	Val	Ser	Ile	Pro	His	Gly	Pro	Asn				
			85					90					95						
Val	Thr	Val	Arg	Ala	Asn	Ile	Ala	Ala	Ile	Thr	Glu	Ser	Asp	Lys	Phe				
			100				105						110						
Phe	Ile	Asn	Gly	Ser	Asn	Trp	Glu	Gly	Ile	Leu	Gly	Leu	Ala	Tyr	Ala				
		115				120						125							
Glu	Ile	Ala	Arg	Pro	Asp	Asp	Ser	Leu	Glu	Pro	Phe	Phe	Asp	Ser	Leu				
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Val	Lys	Gln	Thr	His	Val														
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 <213> Homo sapiens

Pro	Asn	Leu	Phe	Ser	Leu	Gln	Leu	Cys	Gly	Ala	Gly	Phe	Pro	Leu	Asn				
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Gln	Ser	Glu	Val	Leu	Ala	Ser	Val	Gly	Gly	Ser	Met	Ile	Ile	Gly	Gly				
			20					25				30							
Ile	Asp	His	Ser	Leu	Tyr	Thr	Gly	Ser	Leu	Trp	Tyr	Thr	Pro	Ile	Arg				
		35					40					45							

Arg	Glu	Trp	Tyr	Tyr	Glu	Val	Ile	Ile	Val	Arg	Val	Glu	Ile	Asn	Gly
50						55					60				
Gln	Asp	Leu	Lys	Met	Asp	Cys	Lys	Glu	Tyr	Asn	Tyr	Asp	Lys	Ser	Ile
65					70					75				80	
Val	Asp	Ser	Gly	Thr	Thr	Asn	Leu	Arg	Leu	Pro	Lys	Lys	Val	Phe	Glu
				85					90					95	
Ala	Ala	Val	Lys	Ser	Ile	Lys	Ala	Ala	Ser	Ser	Thr	Glu	Lys	Phe	Pro
			100					105					110		
Asp	Gly	Phe	Trp	Leu	Gly	Glu	Gln	Leu	Val	Cys	Trp	Gln	Ala	Gly	Thr
		115					120					125			
Thr	Pro	Trp	Asn	Ile	Phe	Pro	Val	Ile	Ser	Leu	Tyr	Leu	Met	Gly	Glu
	130					135					140				
Val	Thr	Asn	Gln	Ser	Phe	Arg	Ile	Thr	Ile	Leu	Pro	Gln	Gln	Tyr	Leu
145					150					155					160
Arg	Pro	Val	Glu	Asp	Val	Ala	Thr	Ser	Gln	Asp	Asp	Cys	Tyr	Lys	Phe
				165					170					175	
Ala	Ile	Ser	Gln	Ser	Ser	Thr	Gly	Thr	Val	Met	Gly	Ala	Val	Ile	Met
			180					185					190		
Glu	Gly	Phe	Tyr	Val	Val	Phe	Asp	Arg	Ala	Arg	Lys	Arg	Ile	Gly	Phe
		195					200					205			
Ala	Val	Ser	Ala	Cys	His	Val	His	Asp	Glu	Phe	Arg	Thr	Ala	Ala	Val
	210					215					220				
Glu	Gly	Pro	Phe	Val	Thr	Leu	Asp	Met	Glu	Asp	Cys	Gly	Tyr	Asn	Ile
225					230					235					240

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<213> Homo sapiens

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Gly	Ser	Phe	Val	Glu	Met	Val	Asp	Asn	Leu	Arg	Gly	Lys	Ser
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Gly	Gly	Ile	Asp	His	Ser
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Pro	Tyr	Thr	Gln	Gly
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Ser Ser Thr Gly
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